

<110> Zhu, Zhenping

<120> Bispecific Antibodies That Bind to VEGF Receptors

<130> 11245/485762

<140> filed concurrently herewith

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<151> 2002-06-26

<160> 137

<170> WordPerfect 8.0 for Windows

<210> 1

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Trp Ile Asp Pro Glu Asn Gly Asp Ser Gly Tyr Ala Pro Lys Phe Gln
1 5 10 15

Gly
17

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<400> 3

Tyr Tyr Gly Asp Tyr Glu Gly Tyr
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Ser Ala Ser Ser Ser Val Ser Tyr Met His
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Ser Thr Ser Asn Leu Ala Ser
 1 5

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<210> 7
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<400> 7

Gln Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Ser Gly Ala
 1 5 10 15
 Ser Val Lys Leu Ser Cys Thr Thr Ser Gly Phe Asn Ile Lys Asp Phe
 20 25 30
 Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Trp Ile Asp Pro Glu Asn Gly Asp Ser Gly Tyr Ala Pro Lys Phe
 50 55 60
 Gln Gly Lys Ala Thr Met Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
 65 70 75 80
 Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Asn Ala Tyr Tyr Gly Asp Tyr Glu Gly Tyr Trp Gly Gln Gly Thr Thr
 100 105 110
 Val Thr Val Ser Ser
 115

<210> 8
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<400> 8

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Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30
 His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
 35 40 45
 Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60
 Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
 65 70 75 80
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Tyr Pro Phe Thr
 85 90 95
 Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg Ala
 100 105

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 <211> 30
 <212> DNA
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 <212> DNA
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ggc
 Gly
 17 51

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<400> 11

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 Tyr Tyr Gly Asp Tyr Glu Gly Tyr
 1 5 24

<210> 12
 <211> 30
 <212> DNA
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<400> 12

agt gcc agc tca agt gta agt tac atg cac
 Ser Ala Ser Ser Ser Val Ser Tyr Met His
 1 5 10

30

<210> 13
 <211> 21
 <212> DNA
 <213> Mouse

<400> 13

agc aca tcc aac ctg gct tct
 Ser Thr Ser Asn Leu Ala Ser
 1 5

21

<210> 14
 <211> 27
 <212> DNA
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<400> 14

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 Gln Gln Arg Ser Ser Tyr Pro Phe Thr
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27

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 <212> DNA
 <213> Mouse

<400> 15

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 1 5 10 15

48

tca gtc aaa ttg tcc tgc aca act tct ggc ttc aac att aaa gac ttc
 Ser Val Lys Leu Ser Cys Thr Thr Ser Gly Phe Asn Ile Lys Asp Phe
 20 25 30

96

tat atg cac tgg gtg aag cag agg cct gaa cag ggc ctg gag tgg att
 Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45

144

gga tgg att gat cct gag aat ggt gat tct ggt tat gcc ccg aag ttc
 Gly Trp Ile Asp Pro Glu Asn Gly Asp Ser Gly Tyr Ala Pro Lys Phe
 50 55 60

192

cag ggc aag gcc acc atg act gca gac tca tcc tcc aac aca gcc tac
 Gln Gly Lys Ala Thr Met Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
 65 70 75 80

240

ctg cag ctc agc agc ctg aca tct gag gac act gcc gtc tat tac tgt
 Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

288

aat gca tac tat ggt gac tac gaa ggc tac tgg ggc caa ggg acc acg
 Asn Ala Tyr Tyr Gly Asp Tyr Glu Gly Tyr Trp Gly Gln Gly Thr Thr
 100 105 110

336

gtc acc gtc tcc tca
Val Thr Val Ser Ser
115

351

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<213> Mouse

<400> 16

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gag aag gtc acc ata acc tgc agt gcc agc tca agt gta agt tac atg 96
Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
20 25 30

cac tgg ttc cag cag aag cca ggc act tct ccc aaa ctc tgg att tat 144
His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
35 40 45

agc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
50 55 60

gga tct ggg acc tct tac tct ctc aca atc agc cga atg gag gct gaa 240
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
65 70 75 80

gat gct gcc act tat tac tgc cag caa agg agt agt tac cca ttc acg 288
Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Tyr Pro Phe Thr
85 90 95

ttc ggc tcg ggg acc aag ctg gaa ata aaa cgg gcg 324
Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg Ala
100 105

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<211> 15
<212> PRT
<213> Mouse

<400> 17

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
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<210> 18
<211> 45
<212> DNA
<213> Mouse

<400> 18

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<210> 19
<211> 10
<212> PRT

<213> Mouse

<400> 19

Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser
 1 5 10

<210> 20

<211> 15

<212> DNA

<213> Mouse

<400> 20

gggtggaggcg gttca

15

<210> 21

<211> 17

<212> PRT

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<400> 21

Trp Ile Asp Pro Glu Asn Gly Asp Ser Asp Tyr Ala Pro Lys Phe Gln
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Gly
 17

<210> 22

<211> 117

<212> PRT

<213> Mouse

<400> 22

Gln Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Ser Gly Ala
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Ser Val Lys Leu Ser Cys Thr Thr Ser Gly Phe Asn Ile Lys Asp Phe
 20 25 30

Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Trp Ile Asp Pro Glu Asn Gly Asp Ser Asp Tyr Ala Pro Lys Phe
 50 55 60

Gln Gly Lys Ala Thr Met Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
 65 70 75 80

Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Asn Ala Tyr Tyr Gly Asp Tyr Glu Gly Tyr Trp Gly Gln Gly Thr Thr
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Val Thr Val Ser Ser
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<210> 23

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<400> 23

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Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly
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Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
             20             25             30
His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
             35             40             45
Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
             50             55             60
Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
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Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Tyr Pro Phe Thr
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Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
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<210> 25
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 <212> DNA
 <213> Mouse

<400> 25

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tca gtc aaa ttg tcc tgc aca act tct ggc ttc aac att aaa gac ttc 96
Ser Val Lys Leu Ser Cys Thr Thr Ser Gly Phe Asn Ile Lys Asp Phe
             20             25             30
tat atg cac tgg gtg aag cag agg cct gaa cag ggc ctg gag tgg att 144
Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
             35             40             45
gga tgg att gat cct gag aat ggt gat tct gat tat gcc ccg aag ttc 192
Gly Trp Ile Asp Pro Glu Asn Gly Asp Ser Asp Tyr Ala Pro Lys Phe
             50             55             60
cag ggc aag gcc acc atg act gca gac tca tcc tcc aac aca gcc tac 240
Gln Gly Lys Ala Thr Met Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
65             70             75             80

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ctg cag ctc agc agc ctg aca tct gag gac act gcc gtc tat tac tgt 288
 Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

aat gca tac tat ggt gac tac gaa ggc tac tgg ggc caa ggg acc acg 336
 Asn Ala Tyr Tyr Gly Asp Tyr Glu Gly Tyr Trp Gly Gln Gly Thr Thr
 100 105 110

gtc acc gtc tcc tca 351
 Val Thr Val Ser Ser
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 <212> DNA
 <213> Mouse

<400> 26

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gag aag gtc acc ata acc tgc agt gcc agc tca agt gta agt tac atg 96
 Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser Val Ser Tyr Met
 20 25 30

cac tgg ttc cag cag aag cca ggc act tct ccc aaa ctc tgg att tat 144
 His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys Leu Trp Ile Tyr
 35 40 45

agc aca tcc aac ctg gct tct gga gtc cct gct cgc ttc agt ggc agt 192
 Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser
 50 55 60

gga tct ggg acc tct tac tct ctc aca atc agc cga atg gag gct gaa 240
 Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu
 65 70 75 80

gat gct gcc act tat tac tgc cag caa agg agt agt tac cca ttc acg 288
 Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser Tyr Pro Phe Thr
 85 90 95

ttc ggc tcg ggg acc aag ctg gaa ata aaa 318
 Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
 100 105

<210> 27
 <211> 240
 <212> PRT
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<400> 27

Gln Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Ser Gly Ala
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Ser Val Lys Leu Ser Cys Thr Thr Ser Gly Phe Asn Ile Lys Asp Phe
 20 25 30

Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45

Gly Trp Ile Asp Pro Glu Asn Gly Asp Ser Gly Tyr Ala Pro Lys Phe
 50 55 60
 Gln Gly Lys Ala Thr Met Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
 65 70 75 80
 Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Asn Ala Tyr Tyr Gly Asp Tyr Glu Gly Tyr Trp Gly Gln Gly Thr Thr
 100 105 110
 Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Ser Gly
 115 120 125
 Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile Met Ser
 130 135 140
 Ala Ser Pro Gly Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser
 145 150 155 160
 Val Ser Tyr Met His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys
 165 170 175
 Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg
 180 185 190
 Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg
 195 200 205
 Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser
 210 215 220
 Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys Arg Ala
 225 230 235 240

<210> 28
 <211> 238
 <212> PRT
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<400> 28

Gln Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Gly Ser Gly Ala
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 Ser Val Lys Leu Ser Cys Thr Thr Ser Gly Phe Asn Ile Lys Asp Phe
 20 25 30
 Tyr Met His Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Trp Ile Asp Pro Glu Asn Gly Asp Ser Asp Tyr Ala Pro Lys Phe
 50 55 60
 Gln Gly Lys Ala Thr Met Thr Ala Asp Ser Ser Ser Asn Thr Ala Tyr
 65 70 75 80
 Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Asn Ala Tyr Tyr Gly Asp Tyr Glu Gly Tyr Trp Gly Gln Gly Thr Thr
 100 105 110

Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly
 115 120 125

Gly Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Ala Ile Met Ser
 130 135 140

Ala Ser Pro Gly Glu Lys Val Thr Ile Thr Cys Ser Ala Ser Ser Ser
 145 150 155 160

Val Ser Tyr Met His Trp Phe Gln Gln Lys Pro Gly Thr Ser Pro Lys
 165 170 175

Leu Trp Ile Tyr Ser Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg
 180 185 190

Phe Ser Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg
 195 200 205

Met Glu Ala Glu Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Arg Ser Ser
 210 215 220

Tyr Pro Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
 225 230 235

<210> 29
 <211> 43
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic primer

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43

<210> 30
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 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic primer

<400> 30

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30

<210> 31
 <211> 52
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Synthetic primer

<400> 31

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52

<210> 32
 <211> 36
 <212> DNA
 <213> Artificial Sequence

<220>

<223> Signal

<400> 32

tcgatctaga aggatccact cacgttttat ttccag

36

<210> 33
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 <212> PRT
 <213> Artificial Sequence

<220>

<223> leader peptide

<400> 33

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 5 10 15

Val His Ser
 19

<210> 34
 <211> 32
 <212> DNA
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<220>

<223> Synthetic primer

<400> 34

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32

<210> 35
 <211> 11
 <212> PRT
 <213> Mouse

<400> 35

Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His
 1 5 10

<210> 36
 <211> 17
 <212> PRT
 <213> Mouse

<400> 36

Gly Arg Ile Asp Pro Pro Asn Asp Asn Thr Lys Asp Pro Lys Phe Gln
 1 5 10 15

Gly
 17

<210> 37
 <211> 7
 <212> PRT
 <213> Mouse

<400> 37

Pro Pro Phe Tyr Phe Asp Tyr
 1 5

<210> 38
 <211> 11
 <212> PRT
 <213> Mouse

<400> 38

Lys Ala Ser Gln Asn Val Asp Thr Asn Val Ala
 1 5 10

<210> 39
 <211> 7
 <212> PRT
 <213> Mouse

<400> 39

Ser Ala Ser Tyr Arg Tyr Ser
 1 5

<210> 40
 <211> 9
 <212> PRT
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<400> 40

Gln Gln Tyr Asn Ser Phe Pro Tyr Thr
 1 5

<210> 41
 <211> 116
 <212> PRT
 <213> Mouse

<400> 41

Gln Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
 20 25 30

Tyr Ile His Trp Val Lys Gln Ser Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Trp Ile Asp Pro Pro Asn Asp Asn Thr Lys Tyr Asp Pro Lys Phe
 50 55 60
 Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Leu Pro Pro Phe Tyr Phe Asp Tyr Trp Gly His Gly Thr Thr Val
 100 105 110
 Thr Val Ser Ser
 115

<210> 42
 <211> 109
 <212> PRT
 <213> Mouse

<400> 42

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 Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Asp Thr Asn
 20 25 30
 Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile
 35 40 45
 Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly
 50 55 60
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Val Gln Ser
 65 70 75 80
 Glu Asp Leu Ala Glu Tyr Phe Cys Gln Gln Tyr Asn Ser Phe Pro Tyr
 85 90 95
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
 100 105

<210> 43
 <211> 33
 <212> DNA
 <213> Mouse

<400> 43

tct ggc ttc aac att aaa gac acc tat ata cac
 Ser Gly Phe Asn Ile Lys Asp Thr Tyr Ile His
 1 5 10

33

<210> 44
 <211> 51
 <212> DNA
 <213> Mouse

<400> 44

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Gly Arg Ile Asp Pro Pro Asn Asp Asn Thr Lys Asp Pro Lys Phe Gln
1 5 10 15

cag
Gly 51
17

<210> 45

<211> 21

<212> DNA

<213> Mouse

<400> 45

cca ccc ttc tac ttt gac tac 21
Pro Pro Phe Tyr Phe Asp Tyr
1 5

<210> 46

<211> 33

<212> DNA

<213> Mouse

<400> 46

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Lys Ala Ser Gln Asn Val Asp Thr Asn Val Ala
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<210> 47

<211> 21

<212> DNA

<213> Mouse

<400> 47

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Ser Ala Ser Tyr Arg Tyr Ser
1 5

<210> 48

<211> 27

<212> DNA

<213> Mouse

<400> 48

cag caa tat aac agc ttt cct tac acg 27
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<210> 49

<211> 348

<212> DNA

<213> Mouse

<400> 49

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tca gtc aag ttg tcc tgc aca gct tct ggc ttc aac att aaa gac acc Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr 20 25 30	96
tat ata cac tgg gtg aag cag agc cct gaa cag ggc ctg gag tgg att Tyr Ile His Trp Val Lys Gln Ser Pro Glu Gln Gly Leu Glu Trp Ile 35 40 45	144
gga agg atc gat cct ccg aat gat aat act aaa tat gac ccg aag ttc Gly Trp Ile Asp Pro Pro Asn Asp Asn Thr Lys Tyr Asp Pro Lys Phe 50 55 60	192
cag ggc aag gcc act ata aca gca gac aca tcc tcc aat aca gcc tac Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr 65 70 75 80	240
atg cag ctc cgc agc ctg aca tct gag gac act gcc gtc tat tac tgt Met Gln Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Cys 85 90 95	288
gcc ctc cca ccg ttc tac ttt gac tac tgg ggc cat ggc acc acg gtc Ala Leu Pro Pro Phe Tyr Phe Asp Tyr Trp Gly His Gly Thr Thr Val 100 105 110	336
acc gtc tcc tca Thr Val Ser Ser 115	348
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<400> 50	
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gac agg gtc agc gtc acc tgc aag gcc agt cag aat gtg gat act aat Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val Asp Thr Asn 20 25 30	96
gta gcc tgg tat caa cag aaa cca ggg caa tct cct aaa gca ctg att Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys Ala Leu Ile 35 40 45	144
tac tcg gca tcc tac cgg tac agt gga gtc cct gat cgc ttc aca ggc Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg Phe Thr Gly 50 55 60	192
agt gga tct ggg aca gat ttc act ctc acc atc agc aat gtg cag tct Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Val Gln Ser 65 70 75 80	240
gaa gac ttg gca gag tat ttc tgt cag caa tat aac agc ttt cct tac Glu Asp Leu Ala Glu Tyr Phe Cys Gln Gln Tyr Asn Ser Phe Pro Tyr 85 90 95	288

acg ttc gga ggg ggg acc aag ctg gaa ata aaa cgg gcg
 Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
 100 105

327

<210> 51
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<400> 51

Gln Val Lys Leu Gln Gln Ser Gly Ala Glu Leu Val Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr
 20 25 30
 Tyr Ile His Trp Val Lys Gln Ser Pro Glu Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Trp Ile Asp Pro Pro Asn Asp Asn Thr Lys Tyr Asp Pro Lys Phe
 50 55 60
 Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95
 Ala Leu Pro Pro Phe Tyr Phe Asp Tyr Trp Gly His Gly Thr Thr Val
 100 105 110
 Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly
 115 120 125
 Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Lys Phe Met Ser Thr
 130 135 140
 Ser Val Gly Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val
 145 150 155 160
 Asp Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys
 165 170 175
 Ala Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg
 180 185 190
 Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn
 195 200 205
 Val Gln Ser Glu Asp Leu Ala Glu Tyr Phe Cys Gln Gln Tyr Asn Ser
 210 215 220
 Phe Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala
 225 230 235 240

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<400> 52

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tca gtc aag ttg tcc tgc aca gct tct ggc ttc aac att aaa gac acc Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Thr 20 25 30	96
tat ata cac tgg gtg aag cag agc cct gaa cag ggc ctg gag tgg att Tyr Ile His Trp Val Lys Gln Ser Pro Glu Gln Gly Leu Glu Trp Ile 35 40 45	144
gga agg atc gat cct ccg aat gat aat act aaa tat gac ccg aag ttc Gly Trp Ile Asp Pro Pro Asn Asp Asn Thr Lys Tyr Asp Pro Lys Phe 50 55 60	192
cag ggc aag gcc act ata aca gca gac aca tcc tcc aat aca gcc tac Gln Gly Lys Ala Thr Ile Thr Ala Asp Thr Ser Ser Asn Thr Ala Tyr 65 70 75 80	240
atg cag ctc cgc agc ctg aca tct gag gac act gcc gtc tat tac tgt Met Gln Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95	288
gcc ctc cca ccg ttc tac ttt gac tac tgg ggc cat ggc acc acg gtc Ala Leu Pro Pro Phe Tyr Phe Asp Tyr Trp Gly His Gly Thr Thr Val 100 105 110	336
acc gtc tcc tca ggt gga ggc ggt tca ggc gga ggg ggc tct ggc ggt Thr Val Ser Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly 115 120 125	384
ggc gga tgc gac atc gag ctc act cag tct cca aaa ttc atg tcc aca Gly Gly Ser Asp Ile Glu Leu Thr Gln Ser Pro Lys Phe Met Ser Thr 130 135 140	432
tca gta gga gac agg gtc agc gtc acc tgc aag gcc agt cag aat gtg Ser Val Gly Asp Arg Val Ser Val Thr Cys Lys Ala Ser Gln Asn Val 145 150 155 160	480
gat act aat gta gcc tgg tat caa cag aaa cca ggg caa tct cct aaa Asp Thr Asn Val Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ser Pro Lys 165 170 175	528
gca ctg att tac tgc gca tcc tac cgg tac agt gga gtc cct gat cgc Ala Leu Ile Tyr Ser Ala Ser Tyr Arg Tyr Ser Gly Val Pro Asp Arg 180 185 190	576
ttc aca ggc agt gga tct ggg aca gat ttc act ctc acc atc agc aat Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn 195 200 205	624
gtg cag tct gaa gac ttg gca gag tat ttc tgt cag caa tat aac agc Val Gln Ser Glu Asp Leu Ala Glu Tyr Phe Cys Gln Gln Tyr Asn Ser 210 215 220	672
ttt cct tac acg ttc gga ggg ggg acc aag ctg gaa ata aaa cgg gcg Phe Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys Arg Ala 225 230 235 240	720

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Asp Ser Ser Asn Arg Ala Thr
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Ala Ala Ser Ser Leu Gln Thr
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Ser Gly Ser Thr Ser Asn Ile Gly Thr Asn Thr Ala Asn
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Gly
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Val Thr Asp Ala Phe Asp Ile
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Gly Gly Thr Phe Ser Ser Tyr Ala Ile Ser
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<211> 18

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<213> Human

<400> 69

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe
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Gln Gly
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<211> 16

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Gly Tyr Asp Tyr Tyr Asp Ser Ser Gly Val Ala Ser Pro Phe Asp Tyr
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<400> 71

<400> 72

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Ala Arg Gly Tyr Asp Tyr Tyr Asp Ser Ser Gly Val Ala Ser Pro Phe
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 115 120 125

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agg gtc acc atc tct tgt tct gga agc acc tcc aac atc ggt act aat 96
 Arg Val Thr Ile Ser Cys Ser Gly Ser Thr Ser Asn Ile Gly Thr Asn
 20 25 30

act gca aac tgg ttc cag cag ctc cca gga acg gcc ccc aaa ctc ctc 144
 Thr Ala Asn Trp Phe Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
 35 40 45

atc cac aat aat aat cag cgg ccc tca ggg gtc cct gac cga ttc tct 192
 Ile His Asn Asn Asn Gln Arg Pro Ser Gly Val Pro Asp Arg Phe Ser
 50 55 60

ggc tcc aag tct ggc acc tca gcc tcc ctg gcc atc agt ggg ctc cag 240
 Gly Ser Lys Ser Gly Thr Ser Ala Ser Leu Ala Ile Ser Gly Leu Gln
 65 70 75 80

tct gag gat gag gct gat tat tac tgt gca gca tgg gat gac agc ctg 288
 Ser Glu Asp Glu Ala Asp Tyr Tyr Cys Ala Ala Trp Asp Asp Ser Leu
 85 90 95

aat ggc cat tgg gtg ttc ggc gga ggg acc aag ctg acc gtc ctg 333
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 20 25 30

Thr Ala Asn Trp Phe Gln Gln Leu Pro Gly Thr Ala Pro Lys Leu Leu
 35 40 45

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 65 70 75 80

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35 40 45
Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val

50

55

60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Val Thr Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val
 100 105 110

Thr Val Ser Ser
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<211> 321

<212> DNA

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 Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Tyr
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tta gcc tgg tac caa cag aaa cct ggc cag gct ccc agg ctc ctc atc 144
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile
 35 40 45

tat gat tca tcc aac agg gcc act ggc atc cca gcc aga ttc agt ggc 192
 Tyr Asp Ser Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
 50 55 60

agt ggg tct ggg aca gac ttc act ctc acc atc agc agc cta gag cct 240
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80

gaa gat ttt gca act tat tac tgt cta cag cat aac act ttt cct ccg 288
 Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Thr Phe Pro Pro
 85 90 95

acg ttc ggc caa ggg acc aag gtg gaa atc aaa 321
 Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
 100 105

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<213> Human

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Glu Ile Val Met Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
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 20 25 30

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35

40

45

Tyr Asp Ser Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Leu Gln His Asn Thr Phe Pro Pro
 85 90 95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
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<210> 79

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tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttc agt agc tat 96
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30

agc atg aac tgg gtc cgc cag gct cca ggg aag ggg ctg gag tgg gtc 144
 Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

tca tcc att agt agt agt agt agt tac ata tac tac gca gac tca gtg 192
 Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
 50 55 60

aag ggc cga ttc acc atc tcc aga gac aac gcc aag aac tca ctg tat 240
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
 65 70 75 80

ctg caa atg aac agc ctg aga gcc gag gac acg gct gtg tat tac tgt 288
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

gcg aga gtc aca gat gct ttt gat atc tgg ggc caa ggg aca atg gtc 336
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 100 105 110

acc gtc tca agc
 Thr Val Ser Ser 348
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tcg atc acc atc tcc tgc gct gga acc acc act gat ctt aca tat tat 96
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 20 25 30

gac ctt gtc tcc tgg tac caa cag cac cca ggc caa gca ccc aaa ctc 144
 Asp Leu Val Ser Trp Tyr Gln Gln His Pro Gly Gln Ala Pro Lys Leu
 35 40 45

gtg att tat gac ggc aat aag cgg ccc tca gga gtt tct aat cgc ttc 192
 Val Ile Tyr Asp Gly Asn Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60

tct ggc tcc aag tct ggc aac acg gcc tcc ctg aca atc tct gga ctc 240
 Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80

cag gct gag gac gag gct gat tat tac tgc aac tca tat gta agc agc 288
 Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Tyr Val Ser Ser
 85 90 95

agg ttt tat gtc ttc gga act ggg acc aag gtc acc gtc cta 330
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 20 25 30

Asp Leu Val Ser Trp Tyr Gln Gln His Pro Gly Gln Ala Pro Lys Leu
 35 40 45

Val Ile Tyr Asp Gly Asn Lys Arg Pro Ser Gly Val Ser Asn Arg Phe
 50 55 60

Ser Gly Ser Lys Ser Gly Asn Thr Ala Ser Leu Thr Ile Ser Gly Leu
 65 70 75 80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Asn Ser Tyr Val Ser Ser
 85 90 95

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 100 105 110

<210> 82
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tcc ctg aga ctc tcc tgt gca gcc tct gga ttc acc ttc agt agc tat 96
 Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
 20 25 30

agc atg aac tgg gtc cgc cag gct cca ggg aag ggg ctg gag tgg gtc 144
 Ser Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
 35 40 45

tca tcc att agt agt agt agt agt tac ata tac tac gca gac tca gtg 192
 Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
 50 55 60

aag ggc cga ttc acc atc tcc aga gac aac gcc aag gac tca ctg tat 240
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asp Ser Leu Tyr
 65 70 75 80

ctg caa atg aac agc ctg aga gcc gag gac acg gct gtg tat tac tgt 288
 Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

gcg aga gtc aca gat gct ttt gat atc tgg ggc caa ggg aca atg gtc 336
 Ala Arg Val Thr Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val
 100 105 110

acc gtc tca agc 348
 Thr Val Ser Ser
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 20 25 30

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 35 40 45

Ser Ser Ile Ser Ser Ser Ser Ser Tyr Ile Tyr Tyr Ala Asp Ser Val
 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asp Ser Leu Tyr
 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
 85 90 95

Ala Arg Val Thr Asp Ala Phe Asp Ile Trp Gly Gln Gly Thr Met Val
 100 105 110

Thr Val Ser Ser
 115

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gac aga gtc acc atc act tgt cgg gcg agt cag ggt att agt agt cgg 96
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Ser Ser Arg
 20 25 30

tta gcc tgg tat cag cag aaa cca ggg aaa gcc cct aag ctc ctg atc 144
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

tat gct gca tcc agt ttg caa act ggg gtc cca tca agg ttc agc ggc 192
 Tyr Ala Ala Ser Ser Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

agt gga tct ggg aca gat ttc act ctc act atc agc agc ctg cag cct 240
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

gaa gat ttt gca act tac tat tgt caa cag gct aac agg ttc cct ccg 288
 Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Arg Phe Pro Pro
 85 90 95

act ttc ggc cct ggg acc aaa gtg gat atc aaa 321
 Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
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 20 25 30

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 35 40 45

Tyr Ala Ala Ser Ser Leu Gln Thr Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
 65 70 75 80

Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Ala Asn Arg Phe Pro Pro
 85 90 95

Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
 100 105

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<212> DNA

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agg gtc acc atc tcc tgc act ggg agc cac tcc aac ttc ggg gca gga 96
 Arg Val Thr Ile Ser Cys Thr Gly Ser His Ser Asn Phe Gly Ala Gly
 20 25 30

act gat gta cat tgg tac caa cac ctt cca gga aca gcc ccc aga ctc 144
 Thr Asp Val His Trp Tyr Gln His Leu Pro Gly Thr Ala Pro Arg Leu
 35 40 45

ctc att cat gga gac agt aat cgg ccc tcc ggg gtc cct gac cga ttc 192
 Leu Ile His Gly Asp Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
 50 55 60

tct ggc tcc agg tct ggc acc tca gcc tcc ctg gcc atc act ggg ctc 240
 Ser Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
 65 70 75 80

cgg gtt gag gat gag gct gat tat tac tgt cag tcg tat gac tat ggc 288
 Arg Val Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Tyr Gly
 85 90 95

ctg aga ggt tgg gtg ttc ggc ggc ggg acc aag ctg acc gtc ctt 333
 Leu Arg Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

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<212> PRT

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<400> 87

Gln Ser Val Val Thr Gln Pro Pro Ser Val Ser Gly Ala Pro Gly Gln
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 20 25 30

Thr Asp Val His Trp Tyr Gln His Leu Pro Gly Thr Ala Pro Arg Leu
 35 40 45

Leu Ile His Gly Asp Ser Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
 50 55 60

Ser Gly Ser Arg Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
 65 70 75 80

Arg Val Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Tyr Gly
 85 90 95

Leu Arg Gly Trp Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
 100 105 110

<210> 88

<211> 321

<212> DNA

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<400> 88

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gac aga gtc acc atc act tgc cgg gca agt cag aac att aac aac tat 96
 Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Asn Ile Asn Asn Tyr
 20 25 30

tta aat tgg tat caa cag aaa cca gga aaa gcc cct aag ctc ctg atc 144
 Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

tat gct gcc tcc act ttg caa agt ggg gtc cca tca agg ttc agt ggc 192
 Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

agt gga tct ggg aca gat ttc act ctc acc atc acc agc cta cag cct 240
 Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Ser Leu Gln Pro
 65 70 75 80

gaa gat tct gca act tat tac tgc caa cag tat tcc cgt tat cct ccc 288
 Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Arg Tyr Pro Pro
 85 90 95

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 Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Thr
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 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
 35 40 45

Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Thr Ser Leu Gln Pro
 65 70 75 80

Glu Asp Ser Ala Thr Tyr Tyr Cys Gln Gln Tyr Ser Arg Tyr Pro Pro
 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Thr
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<210> 92
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Arg Val Thr Ile Ser Cys Thr Gly Gln Ser Ser Asn Ile Gly Ala Asp
                    20                      25                      30

tat gat gta cat tgg tac cag caa ttt cca gga aca gcc ccc aaa ctc      144
Tyr Asp Val His Trp Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Leu
                    35                      40                      45

ctc atc tat ggt cac aac aat cgg ccc tca ggg gtc cct gac cga ttc      192
Leu Ile Tyr Gly His Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
                    50                      55                      60

tct ggc tcc aag tct ggc acc tca gtc tcc ctg gtc atc agt ggg ctc      240
Ser Gly Ser Lys Ser Gly Thr Ser Val Ser Leu Val Ile Ser Gly Leu
                    65                      70                      75                      80

cag gct gag gat gag gct gat tat tat tgc cag tcc tat gac agc agt      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
                    85                      90                      95

cta agt ggt ttg gta ttc ggc gga ggg acc aag gtg acc gtc cta      333
Leu Ser Gly Leu Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
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                    20                      25                      30

Tyr Asp Val His Trp Tyr Gln Gln Phe Pro Gly Thr Ala Pro Lys Leu
                    35                      40                      45

Leu Ile Tyr Gly His Asn Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
                    50                      55                      60

Ser Gly Ser Lys Ser Gly Thr Ser Val Ser Leu Val Ile Ser Gly Leu
                    65                      70                      75                      80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Ser Ser
                    85                      90                      95

Leu Ser Gly Leu Val Phe Gly Gly Gly Thr Lys Val Thr Val Leu
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 Asp Arg Val Thr Leu Thr Cys Arg Ala Ser Gln Ser Ile Lys Arg Trp
 20 25 30
 tta gcc tgg tat cag cag aaa cca ggg aag gcc cct agg ctc ctc atc 144
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
 35 40 45
 tat gct gca tcc act ttg caa agt ggg gtc cca tca agg ttc agc ggc 192
 Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 ggt gga tct ggg aca gat ttc act ctc acc atc aac agc ctg cag cct 240
 Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
 65 70 75 80
 gaa gat ttt gca att tac tac tgt caa cag gct aac agt ttc cct ccc 288
 Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Pro
 85 90 95
 act ttc ggc cct ggg acc aaa gtg gat atc aaa 321
 Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
 100 105

<210> 97

<211> 107

<212> PRT

<213> Human

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 20 25 30
 Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Arg Leu Leu Ile
 35 40 45
 Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
 50 55 60
 Gly Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Asn Ser Leu Gln Pro
 65 70 75 80
 Glu Asp Phe Ala Ile Tyr Tyr Cys Gln Gln Ala Asn Ser Phe Pro Pro
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 Thr Phe Gly Pro Gly Thr Lys Val Asp Ile Lys
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agg gtc acc atc tcc tgc agt ggg agc agg tcc aac atc ggg gca cac      96
Arg Val Thr Ile Ser Cys Ser Gly Ser Arg Ser Asn Ile Gly Ala His
                    20                      25                      30

tat gaa gtc cag tgg tac cag cag ttt ccg gga gca gcc ccc aaa ctc      144
Tyr Glu Val Val Gln Trp Tyr Gln Gln Phe Pro Gly Ala Ala Pro Lys Leu
                    35                      40                      45

ctc atc tat ggt gac acc aat cgg ccc tca ggg gtc cct gac cga ttc      192
Leu Ile Tyr Gly Asp Thr Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
                    50                      55                      60

tct gcc tcc cac tct ggc acc tca gcc tcc ctt gcc atc aca ggg ctc      240
Ser Ala Ser His Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
                    65                      70                      75                      80

cag gct gag gat gag gct gat tat tac tgc cag tcg tat gac acc agt      288
Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Thr Ser
                    85                      90                      95

cta cgt ggt ccg gtg ttc ggc gga ggg acc aag ctg acc gtc cta      333
Leu Arg Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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                    20                      25                      30

Tyr Glu Val Gln Trp Tyr Gln Gln Phe Pro Gly Ala Ala Pro Lys Leu
                    35                      40                      45

Leu Ile Tyr Gly Asp Thr Asn Arg Pro Ser Gly Val Pro Asp Arg Phe
                    50                      55                      60

Ser Ala Ser His Ser Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Leu
                    65                      70                      75                      80

Gln Ala Glu Asp Glu Ala Asp Tyr Tyr Cys Gln Ser Tyr Asp Thr Ser
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Leu Arg Gly Pro Val Phe Gly Gly Gly Thr Lys Leu Thr Val Leu
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gac aga gtc acc atc act tgt cgg gcg agt cag ggt att gac aac tgg	96
Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Gln Gly Ile Asp Asn Trp	
20 25 30	
tta ggc tgg tat cag cag aaa cct ggg aaa gcc cct aaa ctg atc	144
Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile	
35 40 45	
tac gat gca tcc aat ttg gac aca ggg gtc cca tca agg ttc agt gga	192
Tyr Asp Ala Ser Asn Leu Asp Thr Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	
agt gga tct ggg aca tat ttt act ctg acc atc agt agc ctg caa gct	240
Ser Gly Ser Gly Thr Tyr Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala	
65 70 75 80	
gaa gat ttt gca gtt tat ttc tgt caa cag gct aaa gct ttt cct ccc	288
Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Ala Lys Ala Phe Pro Pro	
85 90 95	
act ttc ggc gga ggg acc aag gtg gac atc aaa	321
Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys	
100 105	

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Leu Gly Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile	
35 40 45	
Tyr Asp Ala Ser Asn Leu Asp Thr Gly Val Pro Ser Arg Phe Ser Gly	
50 55 60	
Ser Gly Ser Gly Thr Tyr Phe Thr Leu Thr Ile Ser Ser Leu Gln Ala	
65 70 75 80	
Glu Asp Phe Ala Val Tyr Phe Cys Gln Gln Ala Lys Ala Phe Pro Pro	
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Thr Phe Gly Gly Gly Thr Lys Val Asp Ile Lys	
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Gly Asp Ser Asn Arg Pro Ser
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Gln Ser Tyr Asp Tyr Gly Leu Arg Gly Trp Val
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Arg Ala Ser Gln Asn Ile Asn Asn Tyr Leu Asn
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Ala Ala Ser Thr Leu Gln Ser
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Gln Gln Tyr Ser Arg Tyr Pro Pro Thr
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Asp Val Thr Ser Arg Pro Ser
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Arg Ala Ser Gln Asp Ile Ser Ser Trp Leu Ala
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Ala Ala Ser Leu Leu Gln Ser
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Gln Gln Ala Asp Ser Phe Pro Pro Thr
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Ala Ala Ser Thr Leu Gln Ser
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Asp Ala Ser Asn Leu Asp Thr
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Gln Gln Ala Lys Ala Phe Pro Pro Thr
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Met Gln Ser Lys Val Leu Leu Ala Val Ala Leu Trp Leu Cys Val Glu
                    5                      10                      15

acc cgg gcc gcc tct gtg ggt ttg cct agt gtt tct ctt gat ctg ccc      155
Thr Arg Ala Ala Ser Val Gly Leu Pro Ser Val Ser Leu Asp Leu Pro
                    20                      25                      30

agg ctc agc ata caa aaa gac ata ctt aca att aag gct aat aca act      203
Arg Leu Ser Ile Gln Lys Asp Ile Leu Thr Ile Lys Ala Asn Thr Thr
                    35                      40                      45

ctt caa att act tgc agg gga cag agg gac ttg gac tgg ctt tgg ccc      251
Leu Gln Ile Thr Cys Arg Gly Gln Arg Asp Leu Asp Trp Leu Trp Pro
                    50                      55                      60

aat aat cag agt ggc agt gag caa agg gtg gag gtg act gag tgc agc      299
Asn Asn Gln Ser Gly Ser Glu Gln Arg Val Glu Val Thr Glu Cys Ser
                    65                      70                      75                      80

gat ggc ctc ttc tgt aag aca ctc aca att cca aaa gtg atc gga aat      347
Asp Gly Leu Phe Cys Lys Thr Leu Thr Ile Pro Lys Val Ile Gly Asn
                    85                      90                      95

gac act gga gcc tac aag tgc ttc tac cgg gaa act gac ttg gcc tcg      395
Asp Thr Gly Ala Tyr Lys Cys Phe Tyr Arg Glu Thr Asp Leu Ala Ser
                    100                     105                     110

gtc att tat gtc tat gtt caa gat tac aga tct cca ttt att gct tct      443
Val Ile Tyr Val Tyr Val Gln Asp Tyr Arg Ser Pro Phe Ile Ala Ser
                    115                     120                     125

gtt agt gac caa cat gga gtc gtg tac att act gag aac aaa aac aaa      491
Val Ser Asp Gln His Gly Val Val Tyr Ile Thr Glu Asn Lys Asn Lys
                    130                     135                     140

act gtg gtg att cca tgt ctc ggg tcc att tca aat ctc aac gtg tca      539
Thr Val Val Ile Pro Cys Leu Gly Ser Ile Ser Asn Leu Asn Val Ser
                    145                     150                     155                     160

ctt tgt gca aga tac cca gaa aag aga ttt gtt cct gat ggt aac aga      587
Leu Cys Ala Arg Tyr Pro Glu Lys Arg Phe Val Pro Asp Gly Asn Arg
                    165                     170                     175

att tcc tgg gac agc aag aag ggc ttt act att ccc agc tac atg atc      635
Ile Ser Trp Asp Ser Lys Lys Gly Phe Thr Ile Pro Ser Tyr Met Ile
                    180                     185                     190

agc tat gct ggc atg gtc ttc tgt gaa gca aaa att aat gat gaa agt      683
Ser Tyr Ala Gly Met Val Phe Cys Glu Ala Lys Ile Asn Asp Glu Ser
                    195                     200                     205

tac cag tct att atg tac ata gtt gtc gtt gta ggg tat agg att tat      731
Tyr Gln Ser Ile Met Tyr Ile Val Val Val Val Gly Tyr Arg Ile Tyr
                    210                     215                     220

gat gtg gtt ctg agt ccg tct cat gga att gaa cta tct gtt gga gaa      779
Asp Val Val Leu Ser Pro Ser His Gly Ile Glu Leu Ser Val Gly Glu
                    225                     230                     235                     240

aag ctt gtc tta aat tgt aca gca aga act gaa cta aat gtg ggg att      827

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Lys	Leu	Val	Leu	Asn	Cys	Thr	Ala	Arg	Thr	Glu	Leu	Asn	Val	Gly	Ile	
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gac	ttc	aac	tgg	gaa	tac	cct	tct	tgc	aag	cat	cag	cat	aag	aaa	ctt	875
Asp	Phe	Asn	Trp	Glu	Tyr	Pro	Ser	Ser	Lys	His	Gln	His	Lys	Lys	Leu	
			260					265					270			
gta	aac	cga	gac	cta	aaa	acc	cag	tct	ggg	agt	gag	atg	aag	aaa	ttt	923
Val	Asn	Arg	Asp	Leu	Lys	Thr	Gln	Ser	Gly	Ser	Glu	Met	Lys	Lys	Phe	
			275				280					285				
ttg	agc	acc	tta	act	ata	gat	ggg	gta	acc	cgg	agt	gac	caa	gga	ttg	971
Leu	Ser	Thr	Leu	Thr	Ile	Asp	Gly	Val	Thr	Arg	Ser	Asp	Gln	Gly	Leu	
			290			295					300					
tac	acc	tgt	gca	gca	tcc	agt	ggg	ctg	atg	acc	aag	aag	aac	agc	aca	1019
Tyr	Thr	Cys	Ala	Ala	Ser	Ser	Gly	Leu	Met	Thr	Lys	Lys	Asn	Ser	Thr	
					310					315					320	
ttt	gtc	agg	gtc	cat	gaa	aaa	cct	ttt	gtt	gct	ttt	gga	agt	ggc	atg	1067
Phe	Val	Arg	Val	His	Glu	Lys	Pro	Phe	Val	Ala	Phe	Gly	Ser	Gly	Met	
				325					330					335		
gaa	tct	ctg	gtg	gaa	gcc	acg	gtg	ggg	gag	cgt	gtc	aga	atc	cct	gcg	1115
Glu	Ser	Leu	Val	Glu	Ala	Thr	Val	Gly	Glu	Arg	Val	Arg	Ile	Pro	Ala	
			340					345					350			
aag	tac	ctt	ggt	tac	cca	ccc	cca	gaa	ata	aaa	tgg	tat	aaa	aat	gga	1163
Lys	Tyr	Leu	Gly	Tyr	Pro	Pro	Pro	Glu	Ile	Lys	Trp	Tyr	Lys	Asn	Gly	
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Ile	Pro	Leu	Glu	Ser	Asn	His	Thr	Ile	Lys	Ala	Gly	His	Val	Leu	Thr	
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Ile	Met	Glu	Val	Ser	Glu	Arg	Asp	Thr	Gly	Asn	Tyr	Thr	Val	Ile	Leu	
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acc	aat	ccc	att	tca	aag	gag	aag	cag	agc	cat	gtg	gtc	tct	ctg	gtt	1307
Thr	Asn	Pro	Ile	Ser	Lys	Glu	Lys	Gln	Ser	His	Val	Val	Ser	Leu	Val	
				405					410					415		
gtg	tat	gtc	cca	ccc	cag	att	ggt	gag	aaa	tct	cta	atc	tct	cct	gtg	1355
Val	Tyr	Val	Pro	Pro	Gln	Ile	Gly	Glu	Lys	Ser	Leu	Ile	Ser	Pro	Val	
			420					425						430		
gat	tcc	tac	cag	tac	ggc	acc	act	caa	acg	ctg	aca	tgt	acg	gtc	tat	1403
Asp	Ser	Tyr	Gln	Tyr	Gly	Thr	Thr	Gln	Thr	Leu	Thr	Cys	Thr	Val	Tyr	
			435				440					445				
gcc	att	cct	ccc	ccg	cat	cac	atc	cac	tgg	tat	tgg	cag	ttg	gag	gaa	1451
Ala	Ile	Pro	Pro	Pro	His	His	Ile	His	Trp	Tyr	Trp	Gln	Leu	Glu	Glu	
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gag	tgc	gcc	aac	gag	ccc	agc	cat	gct	gtc	tca	gtg	aca	aac	cca	tac	1499
Glu	Cys	Ala	Asn	Glu	Pro	Ser	His	Ala	Val	Ser	Val	Thr	Asn	Pro	Tyr	
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cct	tgt	gaa	gaa	tgg	aga	agt	gtg	gag	gac	ttc	cag	gga	gga	aat	aaa	1547
Pro	Cys	Glu	Glu	Trp	Arg	Ser	Val	Glu	Asp	Phe	Gln	Gly	Gly	Asn	Lys	
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att	gaa	gtt	aat	aaa	aat	caa	ttt	gct	cta	att	gaa	gga	aaa	aac	aaa	1595
Ile	Glu	Val	Asn	Lys	Asn	Gln	Phe	Ala	Leu	Ile	Glu	Gly	Lys	Asn	Lys	

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515										520										525																			
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530										535										540																			
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545										550										555										560									
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565										570										575																			
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595										600										605																			
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610										615										620																			
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625										630										635										640									
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690										695										700																			
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705										710										715										720									
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725										730										735																			
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740										745										750																			
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Asn  Asn  Gln  Ser  Gly  Ser  Glu  Gln  Arg  Val  Glu  Val  Thr  Glu  Cys  Ser
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Asp  Gly  Leu  Phe  Cys  Lys  Thr  Leu  Thr  Ile  Pro  Lys  Val  Ile  Gly  Asn
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Ile  Ser  Trp  Asp  Ser  Lys  Lys  Gly  Phe  Thr  Ile  Pro  Ser  Tyr  Met  Ile
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Ser  Tyr  Ala  Gly  Met  Val  Phe  Cys  Glu  Ala  Lys  Ile  Asn  Asp  Glu  Ser
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Tyr  Gln  Ser  Ile  Met  Tyr  Ile  Val  Val  Val  Val  Gly  Tyr  Arg  Ile  Tyr
                    210                     215                     220

Asp  Val  Val  Leu  Ser  Pro  Ser  His  Gly  Ile  Glu  Leu  Ser  Val  Gly  Glu
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Lys  Leu  Val  Leu  Asn  Cys  Thr  Ala  Arg  Thr  Glu  Leu  Asn  Val  Gly  Ile
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Asp  Phe  Asn  Trp  Glu  Tyr  Pro  Ser  Ser  Lys  His  Gln  His  Lys  Lys  Leu
                    260                     265                     270

Val  Asn  Arg  Asp  Leu  Lys  Thr  Gln  Ser  Gly  Ser  Glu  Met  Lys  Lys  Phe
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Leu  Ser  Thr  Leu  Thr  Ile  Asp  Gly  Val  Thr  Arg  Ser  Asp  Gln  Gly  Leu
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Tyr Thr Cys Ala Ala Ser Ser Gly Leu Met Thr Lys Lys Asn Ser Thr
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 Phe Val Arg Val His Glu Lys Pro Phe Val Ala Phe Gly Ser Gly Met
 325 330 335
 Glu Ser Leu Val Glu Ala Thr Val Gly Glu Arg Val Arg Ile Pro Ala
 340 345 350
 Lys Tyr Leu Gly Tyr Pro Pro Pro Glu Ile Lys Trp Tyr Lys Asn Gly
 355 360 365
 Ile Pro Leu Glu Ser Asn His Thr Ile Lys Ala Gly His Val Leu Thr
 370 375 380
 Ile Met Glu Val Ser Glu Arg Asp Thr Gly Asn Tyr Thr Val Ile Leu
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 Thr Asn Pro Ile Ser Lys Glu Lys Gln Ser His Val Val Ser Leu Val
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 Val Tyr Val Pro Pro Gln Ile Gly Glu Lys Ser Leu Ile Ser Pro Val
 420 425 430
 Asp Ser Tyr Gln Tyr Gly Thr Thr Gln Thr Leu Thr Cys Thr Val Tyr
 435 440 445
 Ala Ile Pro Pro Pro His His Ile His Trp Tyr Trp Gln Leu Glu Glu
 450 455 460
 Glu Cys Ala Asn Glu Pro Ser His Ala Val Ser Val Thr Asn Pro Tyr
 465 470 475 480
 Pro Cys Glu Glu Trp Arg Ser Val Glu Asp Phe Gln Gly Gly Asn Lys
 485 490 495
 Ile Glu Val Asn Lys Asn Gln Phe Ala Leu Ile Glu Gly Lys Asn Lys
 500 505 510
 Thr Val Ser Thr Leu Val Ile Gln Ala Ala Asn Val Ser Ala Leu Tyr
 515 520 525
 Lys Cys Glu Ala Val Asn Lys Val Gly Arg Gly Glu Arg Val Ile Ser
 530 535 540
 Phe His Val Thr Arg Gly Pro Glu Ile Thr Leu Gln Pro Asp Met Gln
 545 550 555 560
 Pro Thr Glu Gln Glu Ser Val Ser Leu Trp Cys Thr Ala Asp Arg Ser
 565 570 575
 Thr Phe Glu Asn Leu Thr Trp Tyr Lys Leu Gly Pro Gln Pro Leu Pro
 580 585 590
 Ile His Val Gly Glu Leu Pro Thr Pro Val Cys Lys Asn Leu Asp Thr
 595 600 605
 Leu Trp Lys Leu Asn Ala Thr Met Phe Ser Asn Ser Thr Asn Asp Ile
 610 615 620
 Leu Ile Met Glu Leu Lys Asn Ala Ser Leu Gln Asp Gln Gly Asp Tyr
 625 630 635 640
 Val Cys Leu Ala Gln Asp Arg Lys Thr Lys Lys Arg His Cys Val Val
 645 650 655

Arg Gln Leu Thr Val Leu Glu Arg Val Ala Pro Thr Ile Thr Gly Asn
660 665 670

Leu Glu Asn Gln Thr Thr Ser Ile Gly Glu Ser Ile Glu Val Ser Cys
675 680 685

Thr Ala Ser Gly Asn Pro Pro Pro Gln Ile Met Trp Phe Lys Asp Asn
690 695 700

Glu Thr Leu Val Glu Asp Ser Gly Ile Val Leu Lys Asp Gly Asn Arg
705 710 715 720

Asn Leu Thr Ile Arg Arg Val Arg Lys Glu Asp Glu Gly Leu Tyr Thr
725 730 735

Cys Gln Ala Cys Ser Val Leu Gly Cys Ala Lys Val Glu Ala Phe Phe
740 745 750

Ile Ile Glu Gly Ala Gln Glu Lys Thr Asn Leu Glu
755 760